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No. 4

SHOULD VITAMIN D BE GIVEN ONLY TO INFANTS?

VITAMIN D has been so successful in preventing rickets during infancy that there has been little emphasis on continuing its use after the second year.

But now a careful histologic study has been made which reveals a startlingly high incidence of rickets in children 2 to 14 years old. Follis, Jackson, Eliot, and Park* report that postmortem examination of 230 children of this age group showed the total prevalence of rickets to be 46.5%.

Rachitic changes were present as late as the fourteenth year, and the incidence was higher among children dying from acute disease than in those dying of chronic disease.

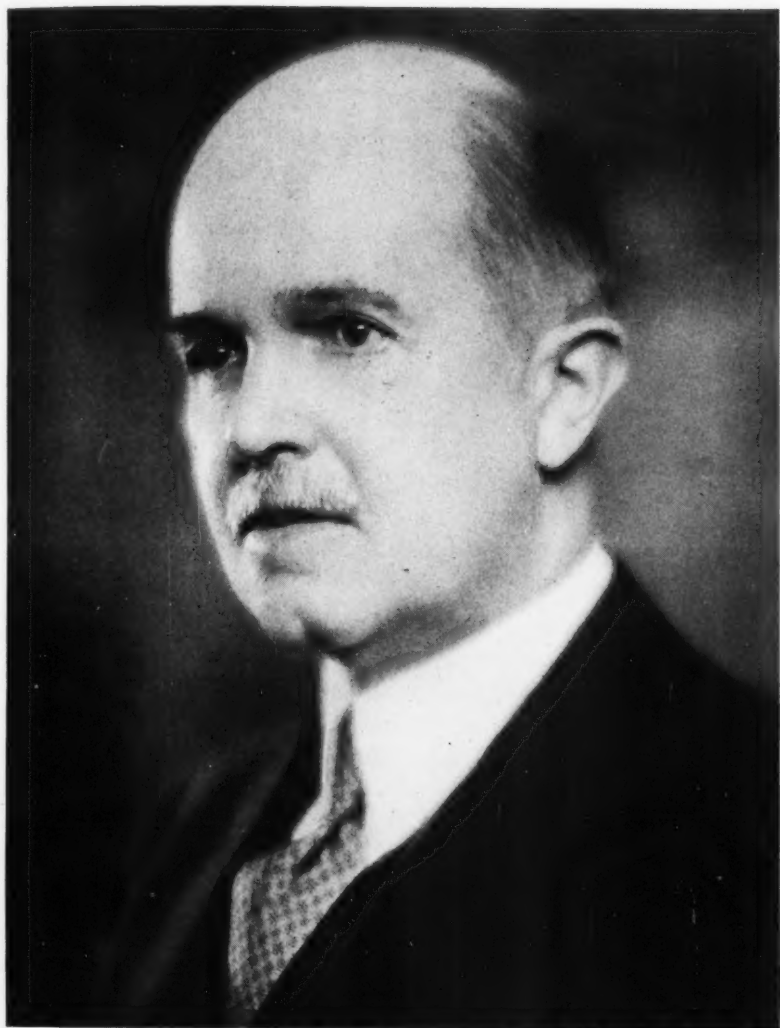
The authors conclude, "We doubt if slight degrees of rickets, such as we found in many of our children, interfere with health and development, but our studies as a whole afford reason to prolong administration of vitamin D to the age limit of our study, the fourteenth year, and especially indicate the necessity to suspect and to take the necessary measures to guard against rickets in sick children."

*R. H. Follis, D. Jackson, M. M. Eliot, and E. A. Park: Prevalence of rickets in children between two and fourteen years of age, *Am. J. Dis. Child.* 66:1-11, July 1943.

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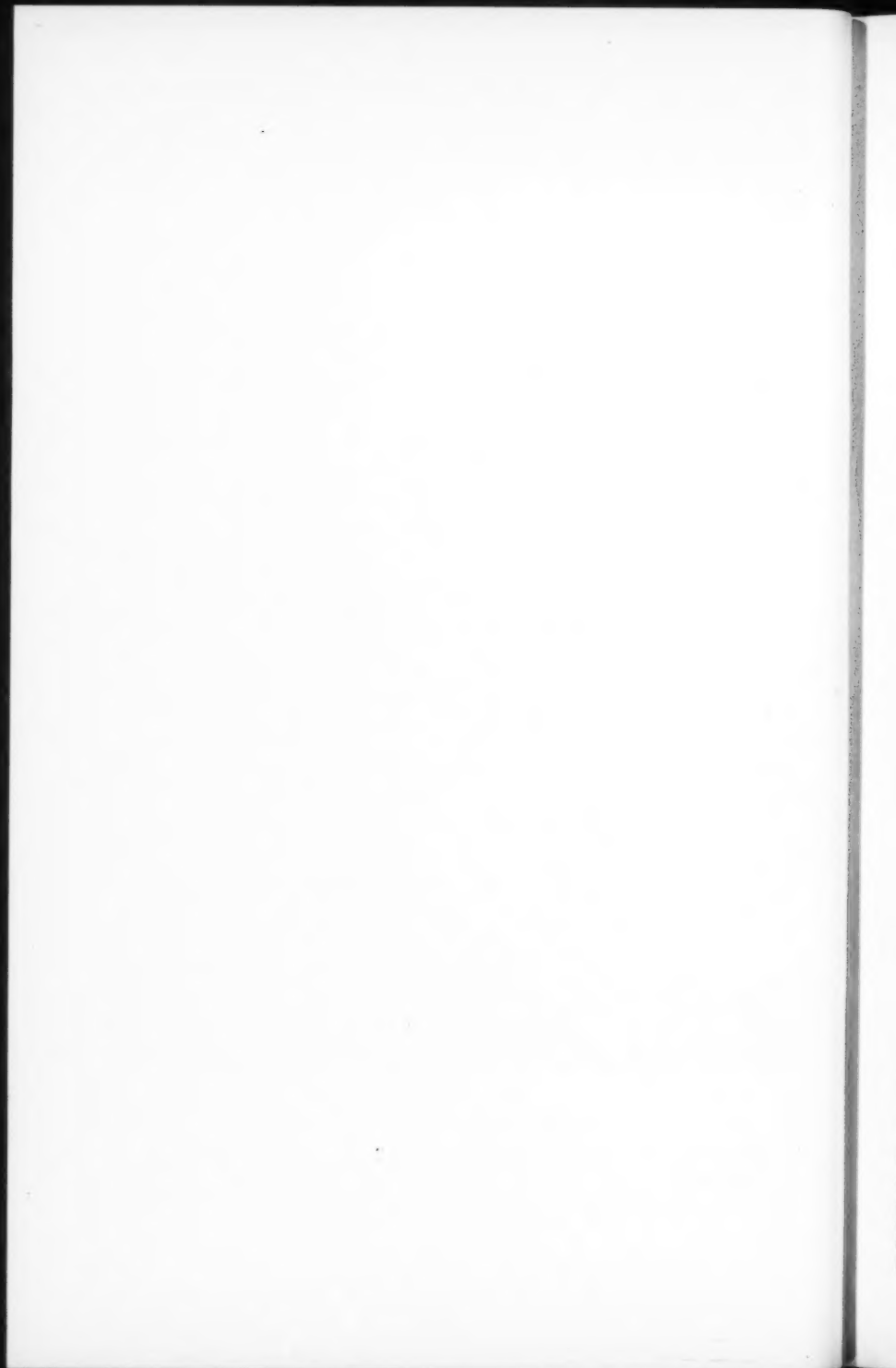


Underwood & Underwood, Washington, D. C.

JOSEPH STILES WALL, M.D.

As an expression of our sincere gratitude for his kindly guidance and wisdom we hereby dedicate this issue of the "Clinical Proceedings" to Dr. Joseph S. Wall, our Chief of Staff, who recently was inaugurated as President of The American Academy of Pediatrics.

THE RESIDENT STAFF.



CASE REPORT NO. 11

CONGENITAL SYPHILIS

Dr. Sidney Ross

GG 44-8437

G. G., a 7 months old white male infant, was admitted to Children's Hospital on November 28, 1944 because of malnutrition and persistent blood tinged nasal discharge of one month's duration.

The patient had been a full term, normal, spontaneous delivery with an uneventful neonatal course. He was progressing moderately well until one month prior to entry, at which time he developed a cough with an attendant nasal discharge which initially was mucoid in character and shortly thereafter, was noted to be blood tinged; this persisted until the time of entry into the hospital. Three weeks before admission, he began to refuse his feedings and had occasional vomiting episodes which resulted in a progressive weight loss. He seemed unusually fretful during this time, his mother describing him as "whining continuously". No history of jaundice or skin lesions was elicited.

One other sibling, aged 3, was presumably in good health. No history of miscarriages or abortions was obtained. The informant, the infant's mother, denied venereal disease in herself, but did relate that her husband had been receiving anti-luetic therapy for an indeterminate period. Social service investigation revealed that this treatment was initiated 7 months ago.

Physical examination showed a pale, marasmic, chronically ill infant. Skin turgor was poor with considerable loss of subcutaneous tissue. There was minimal desquamation around the buttocks and toes and a small condyloma-like lesion was present in the perianal region. No jaundice, fissures, rhagades, or mucoid patches were noted. There was a profuse muco-purulent, blood tinged nasal discharge, with crust formation, producing some nasal obstruction and mouth breathing. The pharynx was mildly injected. Generalized lymphadenopathy was present with palpable cervical, axillary, inguinal and epitrochlear nodes. A soft, blowing grade II apical systolic murmur was heard but the heart was otherwise negative. On examination of the lungs, a few coarse rhonchi were pres-

ent, with harsh breath sounds audible over both bases posteriorly. The abdomen was moderately distended and slightly engorged superficial abdominal veins were noted. The liver was firm and palpably enlarged about 6 cms. below the right costal margin, extending to the iliac crest. The spleen was palpable about 4 cms. below the left costal border. Temperature 100.5°; pulse 120; respirations 30. Physical examination was otherwise essentially negative.

Hemogram showed a red-cell count of 2,750,000 with 5.5 gms. of hemoglobin. The white-cell count was 18,200 with 57% polys. Platelet count was 25,000. Bleeding, clotting, and prothrombin times were within normal range. Fragility test was normal. Van den Bergh test was negative. Icterus index was 6 units. Urinalysis upon entry showed a few white cells and hyaline and granular casts in the sediment but was otherwise negative. Subsequent urinalyses were negative. Both the blood Kahn and Wassermann tests were positive. Spinal fluid examination revealed a positive Wassermann in the 0.5cc dilution, but was negative in the 0.25cc dilution. Colloidal gold curve was 1211110000. Spinal fluid protein and sugar were within normal limits. There was no pleocytosis. The serologic reaction of the patient's mother was found to be positive and she was referred to the Rapid Treatment Center for antiluetic therapy. The serologic reactions of the sibling were negative. Cephalin flocculation test was 4 plus. X-rays of the long bones revealed considerable periostitis and osteo-chondritis which was interpreted as being strongly suggestive of luetic changes. Roentgenographic examination of the lungs was essentially negative.

On the day following entry into the hospital, the infant's temperature rose to 104° and he appeared to be in moderate respiratory distress. He was given sulfadiazine with parenteral fluids and on the following day, the temperature came down to 100°; he continued to show a low grade fever ranging between 100°-102° during the next 5 days, but was afebrile during the subsequent nine week hospital stay.

Because of the marked anemia, the patient received two whole blood transfusions shortly after entry, with a satisfactory rise in hemoglobin. The platelet count which as previously noted, was 25,000 on entry, returned to normal during the first week.

On the 4th day after admission, the patient was started on penicillin antiluetic therapy, the program consisting of 10,000 units every 3 hours intramuscularly on 7 consecutive days for a total dosage of 560,000 units, approximating 50,000 units per pound of body weight.

The subsequent course after the initiation of penicillin therapy can be noted in the accompanying chart.

G.G. — SUMMARY OF COURSE FOLLOWING PENICILLIN THERAPY

Days After Penicillin	Serology		X-Ray-long bones	Cephalin Flocculation	Comment
	Kahn (Units)	Wassermann			
7	120	.1cc. } .05cc. } positive .025cc. } .0125cc. } .00625cc. }	Considerable periostitis and chondritis of all the long bones	4 +	Condition poor; losing weight steadily; liver 6cm. ↓; Spleen 4cm. ↓. Snuffles marked; very fretful
14	240	Positive-all dilutions	Same as above		Condition slightly improved; nutritional status still poor
28	120	Positive-all dilutions	Same as above	4 +	Improved clinically; one pound weight gain in 2 weeks; snuffles subsiding; active and alert. Liver 4cm. ↓. Spleen 3cm. ↓
38	40	.1cc. } .05cc. } positive .025cc. } .0125cc. } doubtful .00625cc. } negative	Marked evidence of healing; some periostitis still present		Condition good. Progressive weight gain continuing. Snuffles no longer present
42	160				Condition remains good; nutritional status satisfactory; appetite excellent
48	40	.1cc.-positive .05cc.-positive .025cc. } .0125cc. } negative .00625cc. }	No change since previous exam. still some periostitis		Improvement continues
62	40				Same as above
72	40	.1cc.-positive .05cc. } .025cc. } negative .0125cc. } .00625cc. }	Only slight residual periostitis		Condition excellent clinically; has gained 5½ lbs. in 10 weeks; alert and active; liver 4cm. ↓; spleen 2cm. ↓
86	4	.1cc.-doubtful .05cc. } .025cc. } negative .0125cc. } .00625cc. }		3 +	Same as above

DISCUSSION:

Major Charles R. Rein *—Individuals with early prenatal or acquired syphilis, may manifest alterations in the spinal fluid constituents. These changes consist in an increase in cells and total protein content, positive serologic reactions for syphilis and variations in the colloidal gold reaction. These features do not necessarily signify that the person has central nervous system syphilis, but indicate that all the organs and tissues of the body are invaded during the early stages of the disease. There is considerable variation in the incidence of such positive spinal fluid findings. Those persons who have positive spinal fluid findings are probably the ones who are more likely to develop clinical nervous system syphilis at a later date. Those who have negative spinal fluids are less likely to develop central nervous system manifestations. Thus the advisability of examining the spinal fluid early is clear. It is worthy of note that a reversal of spinal fluid changes prior to any therapy has been observed in some patients.

The treatment of syphilis with penicillin is still in the developmental stage, but at present, progress is rapid. For the most part, the general methods of therapy with penicillin are equally applicable in children and adults.

Of prime importance in the use of penicillin in the treatment of prenatal syphilis is the avoidance of overzealous treatment. It is far better to initiate treatment with moderate doses and increase the dose after treatment is under way. While no standards have as yet been established, certain groups working on the problem have set up arbitrary guides. One of the larger research groups has put forth some excellent guiding measures. They urge that no more than 20,000 to 30,000 units per pound of body weight be used, believing that this amount is quite adequate. It is believed, however, that larger dosage schedules spread over two or three week intervals will give better results. Further, the total dose is apportioned so that 5% is given on the first day, 10% on the second day, 15% on the third day and no more than 15% per day subsequently. Prolongation of the course of treatment is regarded favorably, for it is the belief that in children the infection is an overwhelming one and should not be treated by rapid methods.

At the present time, the use of a three-hour interval is preferred to a four-hour interval with penicillin. This is because the blood level falls rapidly, a large amount of the drug being eliminated from the blood stream during the first hour after injection. With a four-hour interval there might be a lapse of two to three hours during which the level would be too low and perhaps therapeutically ineffective. The

* Chief of the Division of Serology, Army Medical Center, Washington, D. C.

recent work of Captain Monroe Romansky whereby penicillin is incorporated in a beeswax and peanut oil mixture promises to render frequent administration unnecessary, for satisfactory and prolonged blood levels can be obtained following daily single injections.

The intramuscular and intravenous routes of administration have thus far given the best results. Recent studies indicate that satisfactory blood levels of penicillin may be attained by the oral administration of this antibiotic. There are as yet no definite indications for intra-theal administration. This is true even in children with active central nervous system syphilis, since a satisfactory response may be expected in individuals with marked spinal fluid findings.

It has been observed that the efficacy of penicillin is increased considerably with each degree rise in body temperature. For this reason the use of fever therapy in conjunction with penicillin is being investigated at several research centers.

Serologic response following the institution of therapy have been found to depend on three factors: (1) The stage and severity of the disease at the time treatment was begun; (2) The titre of the serum at the time treatment was started; (3) The type and sensitivity of the tests used. In this regard the less sensitive tests are the first to become negative. It is important to consider all of these factors before attempting to evaluate the progress and success of treatment.

Frequency of blood tests is urged, for by such a procedure the adequacy of treatment can be ascertained. Also, and of tantamount importance, clinical relapses may be anticipated serologically before they appear clinically. The diagnosis of an impending relapse can be made by noting an appreciable and sustained rise in titre. These relapses are prone to occur two or three months after treatment has been discontinued, and by frequent serologic examinations, a relapse may be predicted as long as one month in advance.

The Herxheimer reaction which also occurs with penicillin therapy is of sufficient importance and frequency to warrant attention. The present belief is that it is due to a too rapid destruction of the spirochetes, causing a toxic reaction. Here again the use of smaller doses initially should serve to allay such reactions.

Concerning the serology in newborn infants, it has been observed that syphilitic mothers who have had adequate treatment during pregnancy may give birth to babies with positive serologic reactions for syphilis. Such cases of "syphilotoxemia" do not require treatment. The proper procedure is to perform serological tests on both mother and child at one to two week intervals. The titre of the infant should never exceed that of the mother. If the serologic reactions remain positive after

three months, the presence of syphilis in the infant should be strongly suspected. As a rule the infant's serology becomes negative no later than the third month. It has also been noted that infants with negative serologic reactions at birth may become seropositive at a later date.

The treatment of syphilis during pregnancy is important. Here again smaller initial doses of penicillin are advocated to offset the possibility of placental shock and abortion. Therapy should be started as early as possible but can be instituted at any time during pregnancy, even as late as the 8th month, and be of value. The important thing is to start treatment before the child is born. Anti-syphilitic treatment in the mother may be considered prophylactic up to four and one-half months, for during this time it is given to prevent the fetus from acquiring syphilis. Treatment after $4\frac{1}{2}$ months is abortive, that is, therapeutic, designed to rid the fetus of syphilis.

In conclusion, there are several significant facts which may be drawn from the discussion: Penicillin is very good in treating prenatal syphilis, provided adequate doses are used over a sufficiently long period of time. In the event that positive spinal fluid findings persist, re-treatment is indicated. Institution of treatment during pregnancy is beneficial, even if begun late. The rapidity with which many new uses of penicillin are being unearthed renders standardization of therapeutic procedures impractical at this time.

CASE REPORT NO. 12

FIBROMYXOSARCOMA

Dr. Frederic G. Burke

R.H. - 45-403

R. H., a three year old colored male, was admitted on January 18, 1945, with the chief complaint of a large fungating mass on the right side of the neck and head.

According to the mother, the child had been perfectly well until four months before, when a foul-smelling, brownish discharge was noted oozing from the right ear. He was seen by a private physician who prescribed ear drops and one week later "a piece of red meat" was seen in the right external auditory canal. The mother stated that this mass seemed to grow inward into the canal and two months later she observed a lump about two and one half centimeters in diameter in the mastoid region behind the upper portion of the ear. This mass continued to increase in size. On December 21, 1944, he was taken to the dispensary of Freedman's Hospital, Washington, D. C., and was admitted to the

ward with a diagnosis of acute mastoiditis.* There, a history of being struck by another boy shortly before the onset of symptoms was elicited. The right external canal was filled with a foul muco-purulent discharge and after irrigation a small dark mass was seen extending to the tympanic membrane; the drum itself could not be visualized. A rounded mass about three by five centimeters in size which displaced the right auricle and extended the entire length of the mastoid region to the zygomatic process was noted. This mass was soft, fluctuant, and suggestive of an inflammatory lesion. The skin over the mass was smooth and appeared normal, but the tip of the right mastoid region was quite tender and the skin over it discolored. An X-ray of the mastoid region revealed the presence of a destructive lesion, and a diagnosis of osteomyelitis of the right mastoid bone was made. The hemogram at that time showed 3,500,000 red blood cells, 20,650 white blood cells, and a hemoglobin of 40 percent.

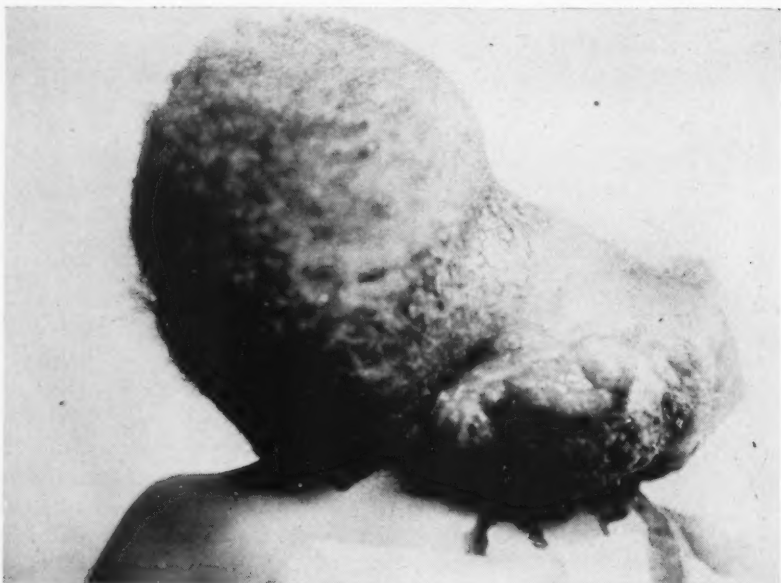
On December 23, 1944 an incision was made over the post-auricular region. The incision extended through the mass which was quite firm. The skin was unusually thin, and the mass extended over the temporal ridge to the squama and to the region of the zygoma. The cortex was partially destroyed. A probe was introduced into the antrum, but no pus was noted. Upon expression of the tumor, a marble-sized polypoid growth which did not exhibit any tendency to bleed was removed from the antrum. Two specimens were sent to the laboratory for examination, and the following report of microscopic examination of these sections was made: the smaller tissue fragments revealed a fibrino-purulent exudate, necrosis, granulation tissue and acanthosis of squamous epithelium. The larger tissues having the gross appearance of polypi revealed a neoplastic growth of stellate elongated cell forms, which varied in size and intensity of nuclear staining and shape. These formed a delicate, edematous, and hemorrhagic stroma supporting thin walled blood vessels. The cells revealed mitoses. The pathological diagnosis was fibromyxosarcoma.

Following operation, the mass rapidly increased in size, growing externally, pushing and stretching the skin. The skin appeared hard and hemorrhagic. Five days post-operatively the mass had attained the size of a baseball.

Palliative measures were employed following the report of malignancy. Surgical removal of the mass was ruled inadvisable because of the type of tumor. On January 14, 1945, the child was removed from Freedman's Hospital against advice.

The following day he was admitted to the Children's Hospital. The past and family histories were non-contributory, and a review of the systems was not remarkable.

* We are indebted to Dr. D. McC. Harper for the summary of the findings and observations made on this patient at Freedman's Hospital, Washington, D. C.

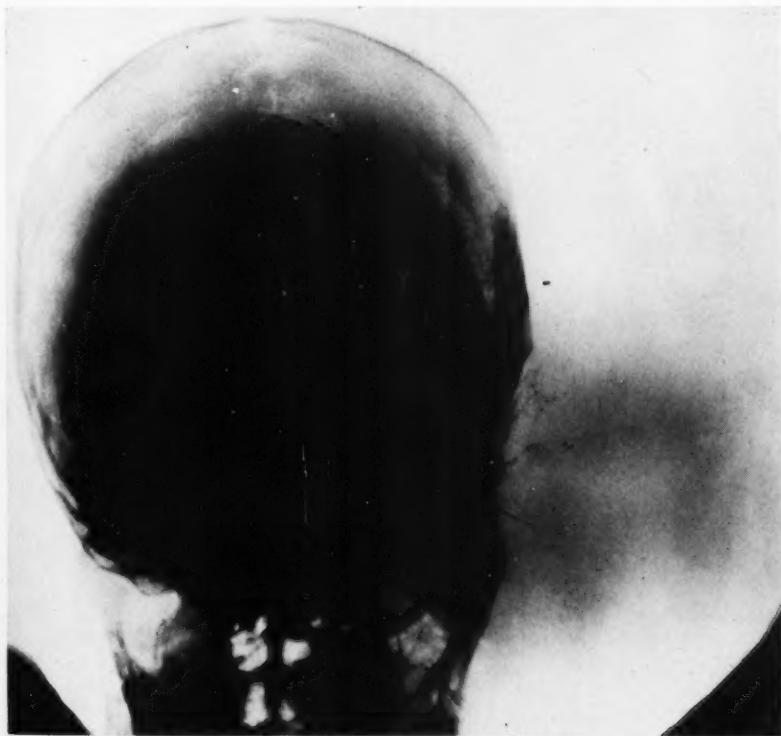


From the Photography Dept., Children's Hospital, Washington, D. C.

R.H. Fibromyxosarcoma of right mastoid bone

Physical examination at that time revealed a moderately anemic colored male, with a huge fungating growth that was quite vascular, malodorous, and necrotic (see illustration). The tonsils were greatly enlarged and inflamed. There was a flaccid paralysis of the right side of the face and the tongue deviated to the right. There was generalized cervical adenopathy. The right ear was displaced forward by the mass in the mastoid region, the left ear was essentially normal. The remainder of the physical examination was essentially negative.

The admitting diagnosis was sarcoma, and x-rays of the skull revealed a destructive lesion in the mastoid portion of the right temporal bone. His temperature on admission was 102° and fluctuated between 99° and 104° during the next five and one-half weeks. Treatment was symptomatic. Blood transfusions were given for the marked anemia and



From the X-Ray and Photography Depts., Children's Hospital, Washington, D. C.

R.H. Fibromyxosarcoma. Note destruction of right Temporal bone by this fungating mass.

codeine sulfate was administered frequently because of pain. X-ray therapy was employed as a symptomatic measure, and a total of eight hundred roentgen units was given anteriorly and laterally, over a period of nine days. This form of therapy was discontinued after this dosage since no beneficial effect was noted.

X-ray examination of the skull after 10 days revealed an increase in the destructive process, and probable involvement of the right mandible was noted. Examination of the long bones of the upper and lower extremities, and of the ribs, failed to show any evidence of metastases. X-ray of the lungs, however, showed an infiltrative lesion in the left base associated with a small amount of fluid. This was thought to represent a bronchopneumonic process, although metastases could not be ruled out. The report of a biopsy of the mass was in agreement with the findings at Freedman's Hospital, namely fibromyxosarcoma.

He pursued a rapidly downhill course, and expired on February 24, five months after the initial appearance of symptoms.

DISCUSSION

Tumors in infants and children are not infrequent occurrences. Very little is known about the factors concerned in their pathogenesis and there is considerable difference of opinion regarding the influence of heredity, trauma, and chronic irritation. Ewing decries the lack of stress in the literature of the fact that benign tumors in this age group of patients far outnumber the malignant types.¹ However, of the malignant tumors, sarcomas are much the commonest type that are seen in childhood. Ninety-seven percent of seven hundred and fifty tumors in children under fifteen years of age observed at the Mayo clinic were sarcomas.¹ However, myxo-sarcomas are curiosities. It is questionable whether true tumors of myxoblastic origin ever exist, since the only place where true myxoblasts are found is in the umbilical cord and in Wharton's jelly. Smith and Gault believe that pure myxomata are not infrequently diagnosed which would be better interpreted as fibromata with extensive myxomatus degeneration of their collagenous stroma.² Pack and Anglem reported a case of a two year old girl observed at the Memorial Hospital, New York, who had a myxo-sarcoma of undetermined histogenesis on the right forearm. The tumor had returned after excision five months before, having increased markedly in size. At the time of amputation of the arm the mass measured 12 x 16 cms. There was no metastasis or evidence of recurrence ten years after treatment.³

The histogenesis in the case just described is not known, but the tumor may have originated in the periosteum of the temporal bone. It is interesting to note that this tremendous growth was nearly all external

and only terminally did it invade the cranial vault. The lack of early metastasis poses the interesting speculation that early wide excision of the tumor might conceivably have been life saving.

¹ Helmholtz, H. F.: Proc. Internat. Assemb. Inter-State Post-Grad. M. A., N. America, p. 210, 1931.

² Smith, L. W. and Gault, E. S., *Essentials of Pathology*, p. 244, D. Appleton Century Co., N. Y., 1942.

³ Pack, G. T. and Anglem, T. J., *Cancer in Childhood*, p. 96, C. V., Mosby Co., St. Louis, Mo., 1940.

⁴ Ewing, J., *Cancer in Children* (Dargeon, H. W.), p. 14, C. V. Mosby Co., 1940.

CASE REPORT NO. 13

"NON-SPECIFIC" PERITONITIS

Dr. Warner

G.R. - 44-8269

J.H. - 44-4693

G. R., a 7 year old white male, was admitted on the evening of 11-19-44 with a complaint of intermittent abdominal pain, listlessness and anorexia of one week's duration. On the day of admission the pain became more severe, and the child experienced some nausea but did not vomit. Bowel movements had been normal during this time. There were no symptoms referable to the respiratory or urinary systems. There was a past history of frequent sore throats and a tonsillectomy. The family history was non-contributory.

Physical examination revealed a well-developed, well-nourished 7 year old white male who appeared listless. The skin was warm and dry. The temperature was 101° rectally. The pharynx was mildly injected. The lungs were clear and the heart was normal. On palpation of the abdomen, tenderness was elicited in both lower quadrants being more marked on the right side. There was no rigidity nor palpable masses. Abdominal reflexes were present. The same distribution of tenderness was found on rectal examination. The white blood count was 7,700 with a predominance of neutrophils. The impression was that of a mild acute appendicitis.

The patient was observed until the next morning at which time the bladder was noted to be distended with the upper border reaching to the level of the umbilicus. The abdomen was soft but tenderness was still present in the lower quadrants. The white-cell count was 8,500 with 74% neutrophils. Urinalysis was negative. Surgical intervention was deemed advisable at this point. When the abdomen was opened, a thick purulent exudate was encountered which was cultured and subsequently found to be sterile. The appendix appeared congested, edematous but non-per-

forated and was removed. No mesenteric adenitis was present. The operative diagnosis was generalized peritonitis. He received parenteral fluids postoperatively for one day, and on the second postoperative day was alert and taking fluids by mouth. Sulfonamides were not administered. The temperature was 100.5° for two days and then returned to normal. He was discharged in seven days after an uneventful postoperative course.

J. H., a $5\frac{1}{2}$ year old colored female, was admitted on the evening of 11-19-44 with the chief complaint of persistent pain in the right side of the abdomen of one day's duration accompanied by two episodes of vomiting. One vomiting attack followed immediately after a dose of milk of magnesia had been given. She had two loose bowel movements on the afternoon of admission. She was drowsy, kept her knees flexed upon the abdomen and refused to eat. Two months before, the patient had had a similar episode of abdominal pain which subsided without incident. The family history was non-contributory.

Physical examination revealed a well developed, well nourished $5\frac{1}{2}$ year old colored female who appeared acutely ill and kept her knees flexed upon the abdomen. Temperature was 101.4° . The tonsils were enlarged but not inflamed. Heart and lungs were negative. Abdominal examination revealed generalized rigidity and tenderness which was more pronounced in the lower right quadrant. There was no rebound tenderness. She was quite tender on both sides on rectal examination, more marked on the right. There were no palpable masses or any vaginal discharge.

The white cell count was 20,000 with 87% neutrophils and 13% lymphocytes. Urinalysis was negative. Red-count and hemoglobin were within normal limits.

A diagnosis of acute appendicitis was made and the patient was operated upon three hours after admission. Upon opening the abdominal cavity, a thick, yellow, odorless material flowed out through the incision. This was cultured. The appendix revealed only congestion of the serosal vessels and was removed. No source of the exudate was found. The operative diagnosis was generalized primary peritonitis.

Following operation, the patient received parenteral fluids and sulfonamide therapy; the latter was discontinued on the following day because of the appearance of gross hematuria. The temperature, which never exceeded 102° , returned to normal on the second postoperative day. Her subsequent course was uneventful and she was discharged on the eighth day. The culture of the peritoneal fluid was negative. Tuberculin test and admission vaginal smear were also negative.

These two cases are presented together because of the similarity of history, physical, operative and laboratory findings and benign post-operative courses. Only one had leucocytosis. Cultures of the peritoneal exudate in both instances were negative. Although the second child received sulfonamide therapy which had to be discontinued within a short time, both had only supportive treatment postoperatively. The rapid and uncomplicated recoveries were rather surprising in view of the large amount of purulent exudate present in the peritoneal cavities in both cases.

CLINICO-PATHOLOGICAL CONFERENCE

Directed by — Dr. E. Clarence Rice

Assisted by — Dr. John E. Cassidy

Held Every Tuesday Afternoon at 3:00 P.M.

R.J. - 44-3280

J.J. - 44-3281

M.J. - 44-3415

Dr. A. A. Levine

R. J., a two year old colored male, was admitted to the hospital on May 9, 1944. He was referred by a county physician from rural Virginia, the home of the patient. The patient and two siblings had been ill for 5 days with a high fever. Richard, the youngest, had an inflamed throat and was quite ill, much more so than the other two. He had vomited two or three times at the onset of the fever which ranged as high as 105°. He had been constipated until the day of admission when he had several loose stools. Listlessness was marked. After sulfonamide therapy had failed to improve his condition, the physician recommended hospitalization.

Physical examination revealed a very sick, comatose, feverish patient with injected ear drums and a greenish curd-like membrane over the tonsils. This exuded a bloody discharge upon removal. The abdomen was markedly distended and the liver and spleen were palpable 2 cm. below the costal margins and quite firm. There was a moderate generalized lymphadenopathy.

A rapid Brahdy culture of the tonsillar membrane produced organisms resembling *Corynebacterium diphtheriae*. The white cell count was 8,200 with 51% neutrophils, 13% of which were young forms, 34% lymphocytes and 2% monocytes. The urinalysis showed 20 mgms. % of albumin and a few hyaline casts.

The patient was given 25,000 units of diphtheria antitoxin on the basis of the throat culture. He was also given sulfadiazine subcutaneously and

supportive measures but failed to show any response and died the day after admission.

Before the necropsy report is given it is important to review the clinical and laboratory findings of the two siblings who fortunately survived.

J. J., a 7 year old brother, was admitted at the same time with a similar history. He also had failed to respond to sulfonamide treatment. The physical findings were almost the same as those of his brother but to a milder degree. The pharynx was inflamed although no tonsillar membrane was present. The abdomen was not distended; the liver and spleen were both palpable 2.5 cm. below the costal margins and were firm. He had a mild generalized non-tender lymphadenopathy. Temperature was 103.6°.

Although the Brahdy culture was negative for *Corynebacterium diphtheriae*, he received 25,000 units of the diphtheria antitoxin in view of his brother's positive throat culture. The hospital course will be reviewed along with that of the third sibling.

M. J., a 10 year old sister, was admitted 4 days after her brothers. Again we have the same history of a continuous high fever and a very ill child. She had a marked pharyngitis and was orthopneic. This girl did not have a palpable spleen or liver but presented a generalized mild non-tender lymphadenopathy. Her throat culture was positive only for streptococci and non-hemolytic staphylococci. The family physician had given her 20,000 units of diphtheria antitoxin on the basis of our findings in the younger brother.

Sulfonamides and supportive therapy were instituted in these older children also but had little effect on the clinical course which was characterized in both by a slow defervescence of temperature and a gradual disappearance of toxicity and listlessness. In both cases the pulse rate was proportional to the fever. The boy developed bronchopneumonia shortly after admission and this persisted for almost three weeks. The girl had a mild bronchitis. The liver and spleen of each decreased in size slowly.

Urinalyses were negative. Repeated white blood counts showed a relative leucopenia. Throat cultures were repeated and were negative for *Corynebacterium diphtheriae*. Stool examinations showed ova of *Ascaris lumbricoides* from both children but were otherwise negative. Wassermann, Kahn and tuberculin tests were negative, as was the blood culture and lumbar puncture in both cases. Agglutination tests for typhoid, salmonella, brucella, and typhus fevers which were carried out shortly after the admissions were negative. Two weeks later, repeat agglutination tests were performed and revealed the following in the boy: the Widal

test was positive in dilutions of 1:640 with *B. typhosus* "O" and 1:160 with *B. typhosus* "H". In the girl there was agglutinations with *B. typhosus* "O" in dilutions of 1:40 and none with *B. typhosus* "H". Heterophile agglutinations were positive in dilutions of 1:112 in the boy and 1:28 in the girl.

In view of the above findings the possibility of typhoid fever was entertained. An investigation of the living conditions by the Social Service Department was carried out to gain more substantial evidence. The family, consisting of the parents and five children, lived on a small farm under very low living standards. The water supply came from an unprotected spring with an adjacent privy across the lane. These conditions served to enhance the growing impression that we were dealing with typhoid fever although the laboratory confirmation was equivocal. Two days after the visiting nurse had given her report on the family life, she recalled the following information volunteered by the parents which she had initially forgotten to submit; the three stricken children had been playing with a dead rabbit found on the premises several days prior to the onset of their illnesses. The mother had cooked the rabbit and the entire family ate it for dinner. Only the three who had played with the rabbit became ill. With this, the diagnosis of tularemia became apparent. Samples of venous blood and sputum of each surviving child were sent to Dr. Larson of the U. S. Public Health Service at Bethesda, Md., and the following significant reports were obtained:

BLOOD

The boy: *P. tularensis* - positive in dilutions of 1:2560

B. abortus - positive in dilutions of 1:1280

The girl: *P. tularensis* - positive in dilutions of 1:2560

B. abortus - positive in dilutions of 1:320

The sputum was injected intraperitoneally into white mice and these animals developed typical signs of tularemia and cultures of *P. tularensis* were obtained.

The two patients remained in the hospital for 50 days and were well on discharge. They have been checked frequently in the Out-Patient Department since then and have remained in good health. Agglutination tests several months after discharge are still positive for *P. tularensis*.

NECROPSY SUMMARY - Dr. John Cassidy

The body of R. J. was that of a well developed and nourished colored male infant weighing eleven kilos. No abnormalities of the skull were noted; clear cisternal fluid was obtained. The cranium was not opened.

The lungs were normal except for some congestion and edema. The

heart showed no abnormalities. The important changes occurred in the intestine, mesenteric lymph nodes and spleen.

The spleen was markedly enlarged, weighing approximately four times that of the normal for a child of this age. The surface was deep purple in color and was studded with many small whitish nodules the average diameter of which was one to two millimeters. The cut surface was firm and was similarly studded. Microscopic examination revealed these to be areas of necrosis surrounded by borders of round cells, fibroblasts, and large mononuclear cells, the cellular reaction being quite limited.

In the gastro-intestinal tract there were other significant findings. The wall of the stomach was studded with irregular grayish areas with excavated central portions where the mucosa was absent. There was no inflammatory reaction about these. Peyer's patches in the terminal ileum were markedly hypertrophic, those near the caecum being cauliflower-like in appearance and almost occluding the lumen. Microscopic examination revealed extensive areas of necrosis in the enlarged patches with a limited cellular reaction, there being a preponderance of mononuclear and round cells. The serosa and muscularis also showed round cell infiltration. The mesenteric lymph nodes were enlarged, those in the region of the terminal ileum and caecum being the largest, measuring 1.5×2.5 cm. Microscopic examination of these nodes showed marked edema and extensive areas of necrosis with some mononuclear cell reaction about them. Remnants of the lymphoid follicles could still be seen.

Pathological diagnosis was pulmonary congestion and edema; marked hyperplasia of Peyer's patches with necrosis; marked mesenteric lymph node enlargement with focal necrosis; splenic tumor with focal necrosis. Cause of death, tularemia.

DISCUSSION:

Dr. E. Clarence Rice: You will realize that we have been talking about an unusual group of cases, unusual in this vicinity because patients with tularemia have rarely died in the hospitals that we have been connected with. So far as is known this is the first child to die of this disease at this hospital. A number of years ago I participated in a necropsy of an adult who died of tularemia. The lesions in the lung and spleen in this patient at first were thought to be tuberculous in nature but subsequent history revealed the patient had dressed a wild rabbit shortly before death.

This child had an illness which was thought to be typhoid fever, largely due to the positive agglutination reactions and the knowledge of the living conditions which surrounded the patient's family. The presence

of organisms thought to be *Corynebacterium diphtheriae* in the smear from the rapid Brahdys throat culture are now believed to have been *Pasturella tularensis* since the morphological appearance of the two are somewhat similar. The positive heterophile antibody reaction is believed to be due to the administration of horse serum (*diphtheria antitoxin*). It is of significance that *Eberthella typhosa* was not isolated from the blood during life or from any of the cultures taken at necropsy.

The lesions in the spleen and mesenteric lymph nodes are typical of tularemia but were not recognized as such at the time. The lack of any significant inflammatory reaction in the surrounding tissues is rather surprising. The lesions in the gut were of a "cauliflower" variety, the masses being sufficiently great to nearly occlude the lower ileum. There were some changes noted in other organs. The kidney showed tubular degeneration. The lungs were edematous and congested but in the sections examined did not give any evidence of pneumonia.

Someone has inquired about the differentiation of these lesions and those found in typhoid fever. It seems to me that the enlargement of the Peyer's patches and the amount of necrosis was greater than one sees in most cases of typhoid fever. At least I have not seen any in the latter disease which approached the extent of these changes.

Later on when the history of a contact with a dead rabbit was known the diagnosis of tularemia was made by positive agglutination tests on the blood from the surviving two children and by the isolation of *Pasturella tularensis* from the sputum by Dr. Larson of the National Institute of Health. Dr. Larson recovered the organism from the sputum of both the surviving children by animal inoculation.

We have all learned a great deal from these cases. No one, so far as I know, considered the diagnosis of tularemia in the case of the patient who died during life or even at necropsy. Most of us will probably never forget to include tularemia as a diagnostic possibility in similar cases in the future.

Question from the floor: Are cross agglutination reactions with *Eberthella typhosa* and *Brucella abortus* usually seen in tularemia?

Dr. Rice: Cross agglutination reactions have been reported with *Brucella abortus* but so far as I know are not ordinarily noted with *Eberthella typhosa*.

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**CLINICAL PROCEEDINGS OF THE
CHILDREN'S HOSPITAL
Washington, D. C.**

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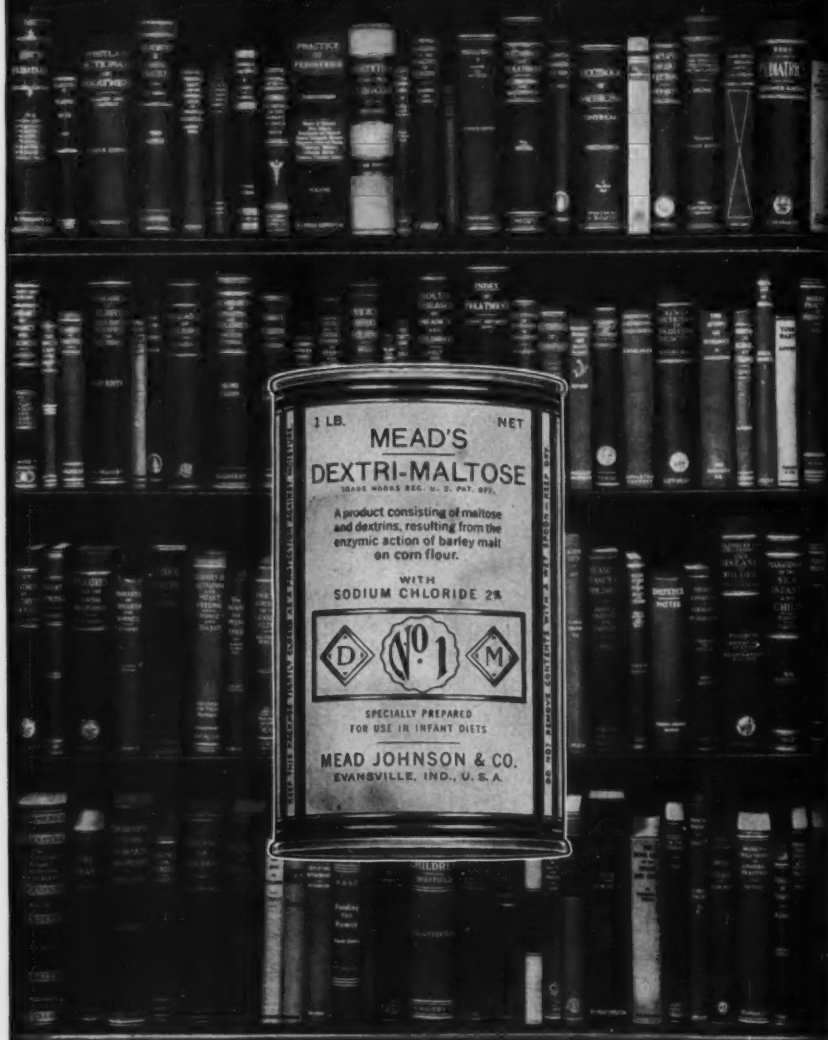
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Occasionally, the remarks and observations of guest speakers are included in this bulletin when thought to have particular interest. The proximity of the Children's Hospital to the Medical Centers of the Army, Navy and United States Public Health Service affords us the opportunity to invite many distinguished physicians to our conferences.

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BACKGROUND



THE use of cow's milk, water and carbohydrate mixtures represents the one system of infant feeding that consistently, for over three decades, has received universal pediatric recognition. No carbohydrate employed in this system of infant feeding enjoys so rich and enduring a background of authoritative clinical experience as Mead's Dextri-Maltose.

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